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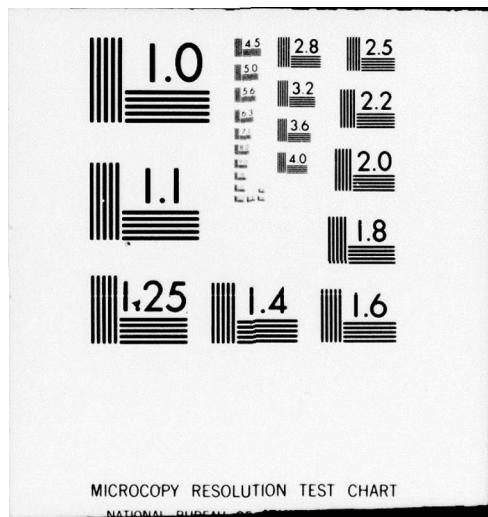
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LOW-POWER LASER ALTERATION OF PHYSIOLOGICAL PROCESSES.(U)
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) The report summarizes a recent analysis of research concerning the alteration or stimulation of biological processes by low-power laser irradiation. A survey of reported studies is given, along with abstracted biomedical case reports. The analysis compares reported laser exposure levels to current safety standards, solar irradiance levels, and exposure levels from published reports of low-level laser effects on visual function. An estimated depth of penetration for the commonly used helium-neon laser is calculated. Thermal modeling was used, with			

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20. ABSTRACT (Continued)

reported laser exposure levels, to estimate the possible contribution of hyperthermia to reported bioeffects. Possible mechanisms are discussed for the coupling of laser energy to cellular processes. Results are correlated to current Air Force research on laser bioeffects.



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LOW-POWER LASER ALTERATION OF PHYSIOLOGICAL PROCESSES

INTRODUCTION

This report summarizes a recent analysis of research concerning laser "biostimulation" (i.e., the stimulation of biological processes by laser radiation). The purpose of this report is to document the sources, concepts, and conclusions of that analysis as well as to correlate it with research on low-level laser effects.

An immediate example will best serve as an introduction to the reported phenomenon of biostimulation. In 1970, Dr. E. Mester of Budapest University published a short report entitled "The Stimulating Effect of Low-Power Laser Rays on Biological Systems" (9). In this report Mester summarized the effects of a ruby laser (694.3-nm wavelength) exposure on eight biological systems. The monitored parameters were:

1. phagocytosis of bacteria by leucocytes
2. catalase activity of leucocytes
3. activity of Ehrlich ascites tumor cells
4. rate of fur growth in mice
5. healing of skin wounds in mice
6. micromotility of intestinal mucosa and villa
7. corneal vascularization induced by adrenal extract
8. synthesis of hemoglobin by bone marrow cells

Mester concluded from his studies that "... exposure to low-energy laser rays stimulates cell function. Exposure to higher energies has resulted in inhibition. Repeated exposures to low doses had a cumulative effect."

The reported phenomenon of biostimulation raises fundamental questions concerning the mechanisms of energy coupling of laser radiation with living tissue. To our own laser researchers such questions are neither unfamiliar nor unexplored; however, to date, most such consideration of energy coupling has been modeled from tissue damage studies.

Use of a simple damage/no-damage model of laser-tissue interaction has successfully led to current laser safety standards. Additionally, several damage mechanisms have been proposed and studied. Some of these mechanisms include the following:

- Thermal denaturation
- Thermal vaporization
- Selective absorption by components/inactivation
- Acoustic or shock-wave transients
- Dielectric membrane breakdown
- Photochemical reactions

Various researchers have sought to refine the damage/no-damage criterion by examining laser-induced changes in smaller and smaller biological units (i.e., from tissue to cellular to subcellular levels). When functional alterations initiated by such changes are considered, the problem inevitably arises of when discovered cellular or subcellular changes are considered "damage" vs. mere "change."

Research concerning biostimulation by low-power lasers emphasizes the fact that laser-induced damage almost certainly exists as a subset of phenomena within the general category of laser-tissue interactions. Thus, if at some level of laser irradiation no damage is being done to a tissue (using whatever realistic criterion of functional damage), we might still expect to find changes brought on by laser-energy deposition. What are the mechanisms of these changes? To what extent are they cumulative? What, if any, are their significant, nondamaging biological effects?

The current analysis began with reports of nondestructive laser-tissue interaction generated in Hungary (9-11) and the Soviet Union (3). These reports proposed that lasers could beneficially accelerate tissue repair processes if properly applied at low power levels. We believe that an examination of this area could lead to new insights and new models of laser-tissue energy coupling which would complement our own work on laser-induced damage. The possibility exists for the development of a more comprehensive understanding of laser-tissue interactions, a firmer basis for safety standards with respect to low-level exposures, and a potential for biomedical applications.

BACKGROUND

The review article "Laser Biomedical Research in the USSR," by Nikolai F. Gamaleya (3), deserves special attention. This is the only comprehensive review of biostimulation (although, admittedly, confined to Soviet research) found in the literature to date. The approach of the cited research is primarily clinical, and the model most extensively used to examine laser-tissue interaction is that of a wound or protracted illness.

The reviewed research on biostimulation can be divided into three categories based on the experimental subject or target, relative to a goal of eventual human applicability. These are:

1. human studies
2. animal studies
3. other studies (e.g., tissue culture or plant systems)

The studies by Soviet workers may also be divided into the following three categories according to type of exposure:

1. direct site exposure (e.g., irradiation of a wound per se)

2. indirect exposure (e.g., irradiation of acupuncture or reflexology points)
3. mixed exposures (i.e., mixed direct and indirect exposures)

Detailed discussion of the merits of these research areas is postponed until the appropriate section of this report. At this stage we will simply document the research which has been reported in the literature. To ease reference to these many studies, a mnemonic coding system (keyed to detailed case reports in the Appendix) is used. Each report is therefore designated by a 2-letter prefix and a number. The first letter refers to the type of exposure: direct (D), indirect (I), or mixed (M). The second letter refers to the experimental subject or target: human (H), animal (A), or other (O). The numerical designation simply denotes the item sequence within any given group. Thus, case report DH-3 is the third cited report in the Appendix concerning direct site exposures with human subjects.

An overview of the types of cases studied is given in Table 1. As can be seen with a review of the case reports in the Appendix, almost all cited studies have used a low-power helium-neon (HeNe) laser, at 632.8-nm wavelength, for exposures. Other laser systems which have occasionally been tried are the ruby laser at 694.3-nm wavelength (DH-7, DA-13), the neodymium (Nd) laser at 1060-nm wavelength (DA-18), and the UV-nitrogen laser at 337.1-nm wavelength (DH-6). Treatment schedules varied greatly, from a single pulse lasting 1 second (DA-9) to a course of treatments lasting 1 hour daily for 25 days or a series of courses lasting up to 6 months (DA-5). Most, but not all (DA-12, IH-5), authors reported some biostimulation of physiological indices or improvement of patient well-being.

Possible mechanisms for a biostimulatory effect have been considered by some authors. Mester and co-workers (10, 11) have been especially prominent in the study of collagen synthesis relative to low-power HeNe and ruby laser biostimulation of wound-healing processes. These workers believe that the basis for the observed effects is an increase in collagen synthesis, possibly resulting from a laser-induced increase in key enzyme activity or an enhanced release of enzyme from storage areas. Electron micrographic studies have implicated, they believe, certain subcellular "vesicles with dense central nuclei" (11). Other researchers support the possibility of collagen-synthesis enhancement by low-power laser irradiation through findings of subcutaneous connective-tissue proliferation in their own studies (DA-1, DA-2, DA-4, DA-18, DH-1).

Some authors have suggested an apparent stimulation of immunologic, defensive reactions of the organism by low-power laser irradiation. Initial mechanisms of energy coupling are not mentioned, but cited secondary evidence includes observations of increased phagocytic activity (DA-2, DH-1, DH-5, DH-14) or an increased progression of inflammatory phases following wounding (DA-4, DA-17).

TABLE 1. AREAS STUDIED WITH DIRECT LASER BIOSTIMULATION

Direct, Human (DH)

Burns: superficial and deep (DH-1)
Wounds: indolent or infected (DH-2, DH-5, DH-6)
Ulcers: trophic, X-ray therapy, posttraumatic (DH-2, DH-3, DH-4, DH-5, DH-6, DH-7)
Fractures (DH-6)
Arthritis (DH-8, DH-9)
Radiculitis (DH-10)
Paralysis (DH-11)
Periodontosis (DH-12, DH-13, DH-14)
Stomatitis (DH-15)

Direct, Animal (DA)

Skin: wounded and unwounded (DA-1, DA-2, DA-16)
Burns (DA-3)
Skin grafts (DA-4)
Prostate (DA-5)
Brain (DA-6)
Sciatic nerve (DA-7)
Pterygopalatine ganglion (DA-8)
Nerve-muscle preparation (DA-9)
Fractures (DA-10, DA-11, DA-12)
Tongue: normal, wounded, or burned (DA-13, DA-14)
Skin: dermatitis or inflammation (DA-15, DA-17)

Gamaleya (3) traces the development of another, controversial general theory for laser-induced biostimulation. This theory dates back to Soviet scientist A. G. Gurvich's theory, in 1944, of "biological field" and "mitogenic radiation," which supposedly act as sources of nonconventional communication between living cells. Gamaleya cites Inyushin, 1972, as modifying this theory with those of Szent-Gyorgi, 1968, into the concept of a total-body "bioplasma," which may be affected by various internal and external factors. According to Inyushin, unfavorable factors could create an instability of the "bioplasma," and such a disturbance would lead to the development of a pathological state. He says that resonance effects of laser radiation, because of its coherence, could return stability to the "bioplasma." With respect to the possibility of a "favorable" resonance, Gamaleya states:

"According to Inyushin and Chekurov (1975), these conditions are satisfied by radiation from a HeNe laser (wavelength 632.8 nm, quantum energy 1.9 eV), during exposure to which migration of quanta takes place in the zones of conductance, with a change in the energetic balance of the organism; this could lead to restoration of its normal physiological state."

Gamaleya acknowledges that this last theory regarding a laser-induced biostimulation of metabolic processes is very open to argument. It is especially attractive, however, to those who wish to provide a theoretical basis of their own reported results using indirect laser exposures (e.g., "laser acupuncture") for curative purposes.

ANALYSIS

The literature surveyed indicates that some mechanism of laser energy coupling to tissue may exist which does not have a net damaging effect. In an attempt to achieve beneficial results, however, scientific rigor has apparently suffered. This analysis will consider some deficiencies of the reported research and attempt to place the reported data in a workable framework.

One immediate consideration is to determine what is meant by a "low-power" laser exposure. None of the cited case reports give detailed laser beam parameters; some do, however, give exposure dose and duration. Using these available data we can calculate an estimated dose per single exposure and compare this value to the current ANSI safety standard for skin exposure (1). This standard is based on a minimal erythremal reaction of the skin, with standards set at levels approximately 1/10 of experimental threshold levels. For the wavelength region of 400-1400 nm, the safety standard is as follows:

For 10^{-9} to 10^{-7} seconds, $MPE = 2 \times 10^{-2} \text{ J/cm}^2$

For 10^{-7} to 10 seconds, $MPE = 1.1 t^{1/4} \text{ J/cm}^2$

For 10 to 3×10^4 seconds, $MPE = 0.2 t \text{ J/cm}^2$

where MPE is the maximum permissible exposure and t is exposure duration in seconds.

Results of the exposure analysis are given in Table 2. As can be seen by the tabulated ratio of reported exposure/ANSI standard, the exposure levels reported in these studies are well below permissible exposure levels.

To gain a better understanding of the power levels used in bio-stimulation experiments, a comparison was made to normal solar radiation levels at sea level. Solar spectral irradiance values (15) for two specific wavelength bands were calculated and modified with a rough 80% atmospheric transmission factor. The three specific cases were (1) $\lambda = 400\text{-}700$ nm (i.e., all visible wavelengths); (2) $\lambda = 625\text{-}635$ nm (i.e., a 10-nm bandwidth near the HeNe laser wavelength); and (3) $\lambda = 632\text{-}633$ nm (i.e., a 1-nm bandwidth at the HeNe laser wavelength).

For $\lambda = 400\text{-}700$ nm, 51.6 mW/cm^2
x80% transmission
 41.3 mW/cm^2 estimated at sea level

For $\lambda = 625\text{-}635$ nm, 1.6 mW/cm^2
x80% transmission
 1.3 mW/cm^2 estimated at sea level

For $\lambda = 632\text{-}633$ nm, $.16 \text{ mW/cm}^2$
x80% transmission
 $.13 \text{ mW/cm}^2$ estimated at sea level

As shown in Table 2, documented animal exposures ranged from 1 to 10 mW/cm^2 and human exposures from 0.1 to 25 mW/cm^2 ; exposure durations in both types of studies ranged from 1 second to several minutes. In comparison to the above calculations, the irradiation levels used by Soviet researchers are generally somewhat greater than normal solar levels if only a small wavelength band is considered. However, experimental irradiations produced less total energy deposition (for equal exposure times) than one would receive from total visible solar irradiation at sea level.

It is, of course, possible that these analyses indicate a wavelength or coherence-dependent effect. Also, subjects receiving laser treatment might have received some other, unintentional preferential treatment which speeded recovery. Ideally, results should be correlated to closely parallel control studies (i.e., identical subject treatment) involving noncoherent light at the wavelength of the laser and at other wavelengths. Shakmeister et al. (see DA-1) did a control experiment with broadband noncoherent light vs. laser exposures in which unwounded, lateral skin areas of rabbits were irradiated. Apparently, as indicated in case report DA-1, they did note differences between coherent and noncoherent light exposures.

TABLE 2. EXPOSURE PARAMETERS AND COMPARISON TO CURRENT ANSI SAFETY STANDARD
FOR CASES OF BIOSTIMULATION DETAILED IN APPENDIX

Case No.	Wavelength (nm)	Exposure per treatment (mW/cm ²)	Duration exposure	Calculated dose per exposure (J/cm ²)	Comparable ANSI standard (J/cm ²)	Ratio: exposure/standard
DA-1	632.8	3.5	5 min	1.05	60 @ 5 min	.0175
DA-2	632.8	2.0*	5 min	1*	60 @ 5 min	.0167
DA-4	632.8	1*	3 min	0.18*	36 @ 3 min	.005
DA-7	632.8	5	5 s	0.025	1.6	.0156
DA-10	632.8	10	1-10 min	6*	120 @ 10 min	.050
DA-11	632.8	6.4	5 min	1.9	60	.0317
DA-15	632.8	3.5	5 min	1.05	60	.0175
-						
DH-1	632.8	0.1	5-10 s	.001*	2	.0005
DH-2	632.8	20*	120 s	2.4*	24	.1
DH-3	632.8	25	90 s	2.25	18	.125
DH-4	632.8	4*	10 min	2.4*	120	.020
DH-8	632.8	12*	1-30 s	0.36*	6 @ 30 s	.060
DH-11	632.8	12	1-several min	2.16	36	.060

*Worst case conditions (i.e., maximum exposure and duration of the experimental range)

Another comparison to be made is with exposures reported to produce low-level laser effects on visual function, since this is an area of current Air Force research interest.

Zwick (17) exposed monkeys to diffusely reflected argon laser (514 nm) irradiation for 2 hours per session daily for at least 16 days. Corneal irradiance was 2.0 W/cm^2 , and calculated retinal irradiance was 0.2 W/cm^2 over the entire retina. Zwick noted a loss of spectral sensitivity in the test animals even though the exposure was far below the safety standard level for extended source exposures. Among other conclusions, he hypothesized a coherence-specific effect as a possible factor in producing low-level laser effects on photoreceptors.

Zwick's reported irradiance level was lower than those shown in Table 2 for biostimulation phenomena; his exposure durations were much longer. Total energy deposition can be calculated as 1.4 mJ/cm^2 , again lower than most values reported in Table 2.

Lawwill et al. (7) exposed monkeys to 4-h exposures of white light or one of four laser lines (514.5 nm, 488 nm, 457.9 nm, or 590 nm). Damage thresholds were monitored through ophthalmoscopic examination, light and electron microscopy, and electroretinography. The authors reported that "minor damage" thresholds of these five exposure conditions were $2-10 \text{ mW/cm}^2$ retinal exposure, with the 457.9-nm line appearing to be the most damaging. Lawwill et al. noted that electroretinogram alterations did not necessarily parallel the overt, histological damage action spectrum (i.e., "damage thresholds" were not equivalent for these two parameters). They concluded that damage was additive (four daily 1-h exposures were equivalent to a single 4-h exposure) and that more than one damage mechanism was in operation.

The exposures of Lawwill et al. were not below current safety standard levels. They were in the range of irradiance values summarized in Table 2; however, duration of exposures used by Lawwill et al. makes the total energy deposition much higher (e.g., 29 J/cm^2 for a 2 mW/cm^2 exposure).

Apparently, functional vision decrements are found at retinal irradiance levels at or below those at which biostimulation effects are noted in other biological systems. Significance of this finding is uncertain, since any attempt to closely correlate exposure levels leading to tissue alterations or mechanisms of action must be approached carefully. This care is needed due to the difficulties in physiologically or physically comparing retina to other tissues when dealing with light effects.

Several problems in analyzing reports on biostimulation arise from their clinical nature. Often the reports tend to be anecdotal, without well-defined experimental parameters, controls, or strong supportive data.

Much of the research has centered only on the healing of wounds or illness. As an experimental model, a wound or state of illness has both advantages and disadvantages. Among the chief advantages is a direct biomedical applicability of results (e.g., research on hyperbaric oxygen enhancement of wound healing). Another advantage is the ease with which some simple wound models can be generated in experimental animals. Disadvantages include the multiplicity and complexity of physiological factors that interplay in the healing process, the lack of controlled models for some wound types (e.g., chronic wounds), the limitation of results to "healing" mechanisms rather than to the normal state (since one is studying an abnormal state by definition), the difficulty in isolating external factors affecting healing, and the problem of objectively quantifying "healing" or "improvement" in some cases. When the subject is human, the physician has a special obligation to alter or terminate the experiment in the best interests of his patient. Also, in a clinical atmosphere, where a wide variety of wounds and ailments are treated, results from many different cases tend to be lumped together.

A factor worth reemphasizing is the need, in a clinical atmosphere, to control conditions so that the only experimental variable is the one intended by the experimenter. The care and hygiene associated with general clinical care might well affect the course of wound healing. Further, when follow-up studies are performed (e.g., as in case DH-12) the importance of patient self-care and hygiene during that period cannot be neglected. Finally, the psychological factor of laser treatment per se cannot be eliminated if dealing with an impressionable patient. Ideally, mock-irradiation or "placebo" studies should be performed unknown to some experimental groups to clarify this factor (e.g., with respect to indirect exposures for the treatment of hypertension).

Unfortunately, not only have different wound types (i.e., test systems) been considered together, but different exposure types (i.e., direct vs. indirect) as well. We believe that the linking of direct and indirect exposures, experimentally or theoretically, is unwise at this time. The most consistent effects, and those which can be studied within the framework of our current physiological knowledge, are those reported with direct exposure of the affected or analyzed tissue. Gamaleya notes that the most dependable results within the direct-exposure group may be those from studies of indolent wounds and trophic ulcers.

One point underlying discussion of low-power laser bioeffects mechanisms is the depth to which laser wavelengths (notably, in this case, the HeNe-generated 632.8 nm) penetrate tissues. More penetrating wavelengths have the potential for generating significant effects at a wider variety of sites or depths. Although absorption data for wounded skin are unavailable at this time, a rough estimate of the anticipated depth of penetration for normal skin can be obtained.

Takata et al. (16) give the nominal thickness of epidermis and dermis as .0121 cm and .1779 cm respectively. They give an absorption coefficient for the outermost .003 cm epidermis (χ_1) as $\approx 26 \text{ cm}^{-1}(\alpha_1)$

and for the remaining skin as $\approx 9 \text{ cm}^{-1} (\alpha_2)$, interpolated from their tabulated data, for the HeNe wavelength. According to the data presented by Takata et al., red wavelengths, as from the HeNe laser, are the most penetrating in the visible spectrum.

The intensity of light (I), relative to the incident beam intensity (I_0), at a depth equivalent to the nominal thickness of the epidermis can be expressed for the HeNe laser as follows:

$$\begin{aligned}\frac{I}{I_0} &= \exp - [(\alpha_1 x_1) + (\alpha_2 x_2)] \\ &= \exp - [(26 \text{ cm}^{-1} \times .003 \text{ cm}) + (9 \text{ cm}^{-1} \times .0091 \text{ cm})] \\ &= 0.85\end{aligned}$$

where x_2 = thickness of epidermis below .003 cm.

In other words, the intensity of the epidermal-dermal interface is still 85% of the initial intensity. Another view of penetration is to consider the total tissue depth, d_1 , at which the incident beam is attenuated by 50% (i.e., $I/I_0 = 0.5$).

$$\begin{aligned}\frac{I}{I_0} = 0.5 &= \exp - [(\alpha_1 x_1) + (\alpha_2 x_2)] \\ &= \exp - [(26 \text{ cm}^{-1} \times .003 \text{ cm}) + (9 \text{ cm}^{-1} \times x_2)]\end{aligned}$$

Solving for x_2 , or d_1 , yields a value of .0683 cm. This indicates that before 50% attenuation occurs, the incident HeNe laser beam has penetrated well into the dermis. This indicates the possibility of HeNe laser bioeffects at several depths or sites.

There are several possible mechanisms through which light, in general, could directly affect tissue processes, wound healing, etc. These include:

1. thermal effects (heating, drying)
2. germicidal effects
3. effects leading to immunological response
4. selective cellular component modification

Niinikoski et al. (12) have indicated that intermittent heating of an open granulating wound by $\approx 3^\circ\text{C}$ during 30-min treatments produced a distinct hyperemia and promoted dry scab formation. Wound closure rate was significantly enhanced.

That such a mechanism might be operative in reported cases of biostimulation was explored by applying a skin thermal model (16) to the exposure parameters detailed in several case reports (DA-1, DA-2, DA-4, DA-10, DA-11, DH-2, DH-3, DH-4). As modeled, in no case did the predicted maximum temperature rise exceed 1°C. This would make a temperature-rise mechanism for biostimulation very unlikely. Still, this is an experimental parameter that must be controlled. Performance of laser irradiations with high-intensity background lighting, or other factors which might warm or dry the wound, could appreciably affect results.

The possibility of a laser germicidal action is indicated in such case reports as DH-4 (alteration of staphylococci sensitivity to antibiotics) and DH-14 (decreased pathogenicity of microorganisms). However, in many instances a biostimulatory effect is reported for noninfected systems. It would be difficult to hypothesize a laser exposure that would directly affect microorganisms without also affecting human cells.

As pointed out by Gamaleya (3), several workers have suggested a laser-induced general activation of the immunological system or a more rapid progression of inflammatory phases in wound healing. The critical mechanism of initial energy coupling is not, however, discussed by those authors. Biostimulation could possibly still be explained for some cases by an initial low-level damage that stimulates the body to respond in a reactive inflammation (DA-10). Alternately, alteration of tissue properties or of immunological system components directly could stimulate or otherwise modulate the immunological reaction.

Mester and co-workers (10, 11), as detailed earlier, have considered the possibility of a laser-induced modification of cellular components. They believe that collagen synthesis is increased by ruby laser activation of a key enzyme or by enhanced release of that enzyme.

Selective absorption of laser radiation leading to component modification is not unusual. Biscar (2) has shown that activity of α -chymotrypsin is greatly increased by near-infrared wavelengths (approximately 850 nm). Rounds (13) has demonstrated that oxygen consumption of tissue cultures can be reduced by laser irradiation with wavelengths that are strongly absorbed by the cytochromes. Indeed, Rounds and co-workers (14) have shown that specific lasers can be used to selectively affect different cytochromes. Hansson (4) has similarly shown that light inhibits oxidative enzymes of the retina. It is interesting that Hunt et al. (5) have suggested that alterations in tissue O_2 could modulate collagen synthesis in wounds. Finally, use of light to treat neonatal jaundice is a common clinical phototherapy. McDonagh and Ramonas (8) have shown that an irradiance of 0.95 mW/cm² (400-520 nm) has a prompt effect on rat bile composition. This is a low-level bioeffect of light, possibly mediated through a direct effect on bilirubin isomerization.

CONCLUSIONS

We conclude that of the cases studied at least some indicate a direct effect of low-power lasers on tissue processes. Results are sometimes obscured by inadequate experimental protocols, inadequate reporting of experimental details, or attempts to correlate widely varying exposure conditions. Still, there is evidence that low-power, nondamaging laser exposures are not biologically inert.

Conventional physiological mechanisms could account for reported cases of laser-induced modification of tissue processes. Details of a feasible energy-coupling mechanism are, however, as yet unknown. Still, there are avenues of research that could clarify the significance of these mechanisms.

Research on low-level effects of laser irradiation, at the tissue level, would be of benefit in several ways. First, a basic understanding could be gained of the nondamaging mechanisms of laser energy coupling with living systems. Potential exists, where mechanisms are defined, of using laser probes to selectively and noninvasively alter tissue function in experimental situations. Second, knowledge of non-damaging mechanisms could impact laser safety standards by clarifying the transition from nondamaging "change" to "damage," a point essential to the concept of damage "threshold." Third, such research would have a direct applicability or correlation to current Air Force low-level laser effects studies. Fourth, the potential for biomedical applications (as pursued by Soviet researchers) cannot be neglected.

Current interest in such potential benefits is by no means confined to the Soviet bloc countries. For example, a Europhysics Conference sponsored by the Italian National Council of Research was held in September 1979 on the topic of "Lasers in Photomedicine and Photobiology." This conference was distinct from a subsequent conference on "Lasers in Bio-Medicine" and, regarding photomedicine, considered only nonsurgical applications of lasers. A portion of the conference on photomedicine and photobiology was devoted to "the fundamental aspects of those processes which can be induced by laser light" (6). Contributed papers included studies on photodynamic therapy, biostimulation effects, photodermatology, photophysiology, and photopharmacology.

The Europhysics Conference is indicative of a growing interest in the physiological actions of laser irradiations and their possible application. We can expect research to continue, as will attempts to take advantage of valid scientific findings through pseudoscientific distortion. A continued survey of literature and developments in this field can provide an input into Air Force programs; however, continuing critical analysis of reported data will be required.

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APPENDIX A. BIOSTIMULATION CASE REPORTS

Case Number Coding: 1st letter = D, I, or M

D = direct exposure of target site

I = indirect exposure via acupuncture, etc., sites

M = mixed (direct & indirect) exposures

2nd letter = A, H, or O

A = animal

H = human

O = other (e.g., cell culture or plant)

Types of Cases to Date: DO

DA

DH

MH

IH

All cases are presented in a uniform format. Missing entries indicate that these data items were not given by Gamaleya (3) or other cited source.

Case Number: D0-1 Type Subject: in vitro
Authors: Shuiskaya (1975 a,b) as cited by Gamaleya, p. 77
Exposure Target: Bone fragments preserved in argon (rabbit bone)
Experimental Controls: Implied, unirradiated
Number of Subjects:
Laser Source: HeNe (25 mW)
Beam Parameters:
Exposure/Treatment:
Duration Exposure: 15 s-1 h per day
Treatment Schedule: Daily for 25 d
Comments: 15-30 s irradiation delayed autolysis, increased alkaline phosphatase activity, and increased redox potential
1-60 min irradiation stimulated autolysis and increased severity of degeneration of osteocytes and ground substance.

Case Number: D0-2 Type Subject: cell culture
Authors: Medvedeva et al. (1974) as cited by Gamaleya, p. 14
Exposure Target: Human kidney and liver tissue
Experimental Controls: Implied, unirradiated
Number of Subjects:
Laser Source: HeNe (25 mW)
Beam Parameters:
Exposure/Treatment:
Duration Exposure:
Treatment Schedule:
Comments: Inhibition of proliferative activity.

Case Number: DA-1 Type Subject: rabbit
Authors: Shakhmeister et al. (1972) as cited by Gamaleya, p. 54
Exposure Target: 2x3-cm lateral skin areas
Experimental Controls: Equivalent exposures of 600-2000-nm noncoherent light
Number of Subjects:
Laser Source: HeNe (15 mW)
Beam Parameters:

Exposure/Treatment: 3.5 mW/cm^2

Duration Exposure: 5 min

Treatment Schedule: 10 times, on alternate days

Comments: Very slight morphological changes: local decreased thickness of stratum granulosum; some dermal leucocyte infiltration; occasional proliferation of fibroblasts with increased RNA and acid mucopolysaccharides in a few cells

Markedly increased aldolase and transaminase activities

No change in cholinesterase activity

Control showed no appreciable change in intermediary metabolism indices.

Case Number: DA-2

Type Subject: rabbit

Authors: Zel'tser et al. (1967) as cited by Gamaleya, p. 54

Exposure Target: 2-cm-diameter circular wound in inner surface of left ear

Experimental Controls: Wounded, but unexposed, right ear

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment: $1.5-2.0 \text{ mW/cm}^2$

Duration Exposure: 5 min

Treatment Schedule: 2 times daily for 1 week

Comments: Data obtained from wound measurements and smear-squash preparations

"Statistically significant acceleration of wound healing" at 1 week

Increased proliferation of connective tissue elements

Increased phagocytosis.

Case Number: DA-3

Type Subject: rat

Authors: Makhmudova (1973) as cited by Gamaleya, p. 55

Exposure Target: Burns

Experimental Controls: Yes, unirradiated

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment: 0.25 mW/cm^2

Duration Exposure:

Treatment Schedule:

Comments: At 1 h to 30 d after first exposure, tested wound redox potential; saw a more rapid rise than in controls.

Case Number: DA-4

Type Subject: rabbit

Authors: Korytnyi (1967, 1969) as cited by Gamaleya, pp. 55,56

Exposure Target: Full-thickness skin grafts transplanted from right thigh to right cheek

Experimental Controls: Yes, unirradiated

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment: $0.5-1 \text{ mW/cm}^2$

Duration Exposure: 3 min

Treatment Schedule: Donor area irradiated 2 times daily for 7-10 d, then 10 more days after autograft

Comments: Smoother appearance and less visible scars

Growth of hair resumed sooner

More rapid infiltration of neutrophils (polymorphs) vs. plasma cells (Korytnyi interprets this as an increased progression of inflammatory phases)

Decreased fibrin accumulation in early healing stages

Increased development of fibroblasts, connective-tissue cells

Decreased depth of spread of necrotic zone

Initially slowed restoration of epidermis, but more rapid final formation

Increased DNA and glycogen synthesis in epidermis until epithelialization rate increased.

Case Number: DA-5

Type Subject: dog

Authors: Svidler and Elunin (1974) and Kozlov and Elunin (1974) as cited by Gamaleya, pp. 67, 68

Exposure Target: Exposed prostate gland, injected with dyes as photosensitizers

Experimental Controls:

Number of Subjects: 20

Laser Source: HeNe (20 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 2-30 min, increasing with number of treatments

Treatment Schedule: Every 2 or 4 weeks for 6 months

Comments: No necrotic changes

Healing by first intention

Glandular proliferation (authors conclude laser can stimulate glandular function).

Case Number: DA-6

Type Subject: rabbit

Authors: Chechulin et al. (1973) as cited by Gamaleya, pp. 70, 71

Exposure Target: Sensorimotor cortex of brain irradiated through skull, with skin reflected

Experimental Controls: Irradiation of forelimb

Number of Subjects:

Laser Source: HeNe (15 W cited; may be 15 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 5, 10, or 30 min per day

Treatment Schedule: Daily for 10 d

Comments: Desynchronization of sensorimotor EEG, on morning after irradiation, for long exposures (no change with 5-min exposure)

As sessions progressed, noted increased delta activity (high amplitude, 0.8-3 Hz)

No comparable changes seen in controls.

Case Number: DA-7

Type Subject: rat

Authors: Rakhishev and Tsoi (1972, 1973) as cited by Gamaleya, p. 71

Exposure Target: Right sciatic nerve severed and joined by epineurial suture--irradiated outer surface of thigh in area of projection of the nerve division

Experimental Controls: Yes, unirradiated

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment: 5 mW/cm²

Duration Exposure: 5 s

Treatment Schedule: 15 d

Comments: By 45 d, saw increased degree neurotization of scar zone and number of nerve fibers growing into peripheral segments

Decreased threshold current for excitability

Authors concluded "a stimulating action on regeneration."

Case Number: DA-8

Type Subject: cat

Authors: Rakhishev et al. (1971) as cited by Gamaleya, p. 71

Exposure Target: Pterygopalatine ganglion irradiated in situ (this is a peripheral nerve center supplying lacrimal gland and nasopalatine mucous membrane)

Experimental Controls: Yes, unirradiated

Number of Subjects:

Laser Source: HeNe (5 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 30 s and 3 min

Treatment Schedule: Single exposure

Comments: Measured intensity of "electrobioluminescence" (EBL) to determine effects on electrophysiological state of nerve tissue

30-s exposure decreased EBL by 40-50%

3-min exposure increased EBL by 120-160%.

Case Number: DA-9

Type Subject: spring frog

Authors: Ratsbaum and Boiko (1973) as cited by Gamaleya, p. 72

Exposure Target: Sciatic nerve-gastrocnemius muscle preparation in moist chamber--time constant of accommodation was determined with Ag-AgCl electrodes and an accommodometer-chronaximeter

Experimental Controls:

Number of Subjects:

Laser Source: HeNe (0.5 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 1 s-12 h

Treatment Schedule: Continuous, single exposure

Comments: No alteration of time constant of accommodation at 1 h

Increased time constant of accommodation at 2 h with later increased rate of accommodation (i.e., "biphasic changes in the accommodative power of nerve")

Authors conclude that no severe pathobiotic changes occurred.

Case Number: DA-10

Type Subject: dog

Authors: Chekurov (1971 a & b, 1972) as cited by Gamaleya, pp. 76, 77

Exposure Target: Fractured radius in cast with optical window to skin opposite wound

Experimental Controls: Yes, unirradiated

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment: 10 mW/cm^2

Duration Exposure: 1 min or 10 min per day

Treatment Schedule: Daily for 30 d

Comments: Initial edema increased with higher dose

More rapid development of bony callus

More rapid total healing

Authors postulate laser-stimulated reactive inflammation, increased blood flow, and more rapid progression of regenerative phases.

Case Number: DA-11

Type Subject: rabbit

Authors: Gorpinko and Gavrilov (1973) as cited by Gamaleya, p. 77

Exposure Target: Resected upper tibia with homograft of periosteum

Experimental Controls:

Number of Subjects:

Laser Source: HeNe (20.4 mW)

Beam Parameters:

Exposure/Treatment: 6.4 mW/cm^2

Duration Exposure: 5 min

Treatment Schedule: 5-20 sessions
Comments: "Stimulated bone regeneration."

Case Number: DA-12 Type Subject: rabbit
Authors: Bogdanovich et al. (1972) as cited by Gamaleya, p. 77
Exposure Target: Resected 0.5-cm segment of middle third of diaphysis of fibula after dividing muscles and stripping the periosteum
Experimental Controls: Yes, unirradiated
Number of Subjects:
Laser Source: HeNe (10 mW)
Beam Parameters:
Exposure/Treatment:
Duration Exposure: 5 min
Treatment Schedule: 2-4 courses, each of 13-15 sessions
Comments: Some pseudoarthrosis in both groups; remaining animals healed in 60-90 d regardless of exposure
Blood tests: Decreased blood Ca^{2+} , pH, and sialic acids; inhibition of alkaline phosphatase; decreased albumin concentration and leukocyte count
Authors conclude that blood changes with laser are "unfavorable."

Case Number: DA-13 Type Subject: rat
Authors: Fokin (1971) and Kurlyandskii et al. (1972) as cited by Gamaleya, pp. 80, 81
Exposure Target: Tongue wound (5-mm diameter x 1-mm deep)
Experimental Controls: Yes, unirradiated
Number of Subjects:
Laser Source: Ruby or HeNe
Beam Parameters:
Exposure/Treatment: 1.5-53 J
Duration Exposure:
Treatment Schedule: Single exposure 24 h after wounding
Comments: Histologically, irradiated group had some superimposition of laser injury on the wound (i.e., a larger damage area)

Controls began epithelialization sooner but continued longer
Authors conclude a definite laser-induced stimulation of repair.

Case Number: DA-14

Type Subject: rat

Authors: Korytnyi et al. (1970), Korytnyi (1971a), Kurythyi and Askarova (1974), and Baigurina (1971) as cited by Gamaleya, pp. 81, 82

Exposure Target: Tongue, normal and burned

Experimental Controls: Yes, unirradiated

Number of Subjects:

Laser Source: HeNe (#1 = 1.4 mW, CW)(#2 = 12 mW, CW or pulsed)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: Laser #1--15 s-3 min, CW

Laser #2--5 s-10 min, CW; 950- and 1900-s pulsed exposure (equiv. to 5 and 10 s, CW)

Treatment Schedule: 1 or 5 exposures

Comments: Hyperemia and slight edema of intact irradiated tissues initially with degenerative changes at \geq 10 min with 12 mW

Irradiation produced faster necrotic sloughing and epithelialization of burns, with low doses more effective (i.e., \leq 1/min at 12 mW). Irradiation for 10 min produced degenerative changes

Irradiation also decreased absorption of neutral red dye and increased H₂O absorption (possibly indicative of decreased denaturation)

Saw no significant difference with CW vs. pulsed laser exposure on normal tissue, but pulsed irradiation had a "more marked stimulating effect" for burns

These results served as the basis for a clinical application to stomatitis (Korytnyi, 1976b).

Case Number: DA-15

Type Subject: dogs and rabbits

Authors: Chechulin et al. (1972, 1973) as cited by Gamaleya, pp. 84, 85

Exposure Target: Dogs = skin region with dermatitis caused by dinitro-chlorobenzene

Rabbits = 2x3-cm intact area on side (tested for blood changes)

Experimental Controls: Yes, implied

Number of Subjects:

Laser Source: HeNe (15 mW)

Beam Parameters:

Exposure/Treatment: 3.5 mW/cm^2

Duration Exposure: 5 min per session

Treatment Schedule: 10 times, on alternate days

Comments: At 5 sessions: decreased Hb concentrations; decreased number of rbc, wbc, and platelets (within wbc saw decreased lymphocytes, but increased monocytes and eosinophils)

At 10 sessions: peripheral blood indices had returned to normal except a 5.4% decrease in lymphocytes

Interim change in clotting system: increased formation of thromboplastin, thrombin, and fibrin; accelerated fibrin-platelet clotting; decreased retraction time; enhanced fibrinolysis. Prothrombin complex activity decreased 11%; recalcification time decreased 20%; free heparin concentration decreased 17%

In dogs, platelet contact activity increased 61% and adhesive activity increased 65%

Saw some return of clotting factors to normal by 10 sessions.

Case Number: DA-16

Type Subject: rabbits

Authors: Shakhtmeister et al. (1973) as cited by Gamaleya, p. 85

Exposure Target: Intact area on side (as DA-15); tested blood serum

Experimental Controls: Implied

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment:

Duration Exposure:

Treatment Schedule:

Comments: Decreased concentration of total proteins, albumins, and sugar in serum

Increased activity of aldolase, glutamate-aspartate transaminase, glutamate-alanine transaminase, and cholinesterase.

Case Number: DA-17

Type Subject: rabbits

Authors: Sokolova and Bocko (1973) as cited by Gamaleya, pp. 114,115

Exposure Target: Irradiated rabbits "in which inflammation had been produced by the subcutaneous injection of turpentine"

Experimental Controls: Implied, unirradiated
Number of Subjects:
Laser Source: HeNe
Beam Parameters:
Exposure/Treatment:
Duration Exposure:
Treatment Schedule:
Comments: Aggravation of the course of the inflammation
"Reduced reactivity of the irradiated animals."

Case Number: DA-18 Type Subject: mice
Authors: Tsyganova (1973 a,b) as cited by Gamaleya, p. 148
Exposure Target:
Experimental Controls:
Number of Subjects:
Laser Source: Nd
Beam Parameters:
Exposure/Treatment: 10.2 J/cm^2
Duration Exposure:
Treatment Schedule:
Comments: Stimulated "proliferation of subcutaneous connective tissue."

Case Number: DH-1 Type Subject: human
Authors: Kovinskii (1973) and Kovinskii et al. (1974) as cited by Gamaleya,
p. 116
Exposure Target: Gp 1 = superficial burns (degrees II and IIIa)
Gp 2 = deep burns (degrees IIIb and IV)
Experimental Controls: Gp 3 = Both burn types; no irradiation, but
received normal clinical burn treatment
Number of Subjects: 12/group
Laser Source: HeNe
Beam Parameters:
Exposure/Treatment: 0.1 mW/cm^2
Duration Exposure: 5-10 s per session
Treatment Schedule: 10 times, on alternate days (Gp 2 was autografted at
5 sessions and treatments continued)

Comments: After 5 sessions: increased granulation and epithelization; increased neutrophils in exudate; decreased plasma cells and polyblasts

In Gp 1, additionally, fibroblasts and fibrocytes appeared and phagocytosis increased vs. control.

Case Number: DH-2

Type Subject: human

Authors: Shchur et al. (1971) and Shchur and Makeeva (1972) as cited by Gamaleya, pp. 116, 117

Exposure Target: Indolent infected wounds and trophic ulcers, 1 mo-25 yr duration (15 = postoperative; 6 = trauma)

Experimental Controls:

Number of Subjects: 21

Laser Source: HeNe (20 mW)

Beam Parameters: Varied spot from 0.2-70 cm²

Exposure/Treatment: 0.2-20 mW/cm²

Duration Exposure: 0.1-120 s at several sites (total session = 20 s to a few minutes)

Treatment Schedule: Daily, with increased dose

Comments: Most had granulation and epithelization in 3 to 5 d; general condition improved, pain was relieved, and sleep was restored

In 17/21 healing was complete after 12-23 d

In 2/21 healing was complete after 43 d

With 1/21 healing was not complete

And 1/21 quit the study

Blood and urine tests showed "no adverse effects" on general blood, clotting system, or kidney function.

Case Number: DH-3

Type Subject: human

Authors: Durmanov and Akhmetov (1973) as cited by Gamaleya, p. 117

Exposure Target: X-ray therapy ulcers, 1-9-yr duration and 2-5-cm-diameter size

Experimental Controls:

Number of Subjects: 5

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment: 25 mW/cm²

Duration Exposure: 1.5 min

Treatment Schedule: 20 daily sessions

Comments: "Cured."

Case Number: DH-4

Type Subject: human

Authors: Babayants et al. (1972, 1974), Devyatkov et al. (1963), Rakcheev (1973) as cited by Gamaleya, pp. 117, 118

Exposure Target: Skin ulcers of 1-40 yr duration

Gp 1 = trophic varicose ulcers

Gp 2 = posttraumatic ulcers

Gp 3 = ulcerative allergic vasculitis

Experimental Controls: Trophic ulcers treated with vitamins and ointments

Number of Subjects: Gp 1 = 55, Gp 2 = 33, Gp 3 = 21, Control = 26

Laser Source: HeNe

Beam Parameters: Spot size = 5 cm²

Exposure/Treatment: 4 mW/cm²

Duration Exposure: 3 min to 8 or 10 min (increased with time); large ulcers were exposed in sections

Treatment Schedule: Daily for 25-30 d

Comments: 73/109 cured (i.e., wound healed without scar) vs. 6/26 control

35/109 improved (i.e., granulation formation, 60-70% epithelialized, decreased pain) vs. 18/26 control

1/109 unimproved vs. 2/26 control

Best results were with varicose ulcers and ulcerative vasculitis

Mean duration treatment = 36.1 d laser vs. 47.5 d control

Saw increased number rbc, decreased rbc sedimentation rate, decreased number wbc, decreased prothrombin index, increased total protein, decreased bleeding and clotting times, increased immunoglobulins of YM type

Wound staphylococci altered sensitivity to antibiotics but not pathogenic properties

Follow-up indicated recurrence in 8/58 interviewed subjects.

Case Number: DH-5

Type Subject: human

Authors: Bogdanovich et al. (1973, 1974) as cited by Gamaleya, p. 118

Exposure Target: Infected wounds and ulcers (irradiation was concentrated on the periphery)

Experimental Controls:

Number of Subjects: 49

Laser Source: HeNe (10 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 10 min/site (<30 min/session)

Treatment Schedule: 12-15 sessions

Comments: After 3-5 sessions edema disappeared, epithelization increased, granulation increased, and discharge decreased and changed in composition

After treatment the number of microorganisms and pathogenicity decreased

Also, saw increased phagocytosis, with increased number of monocytes and macrophages

No detrimental effects on blood noted

No decreased phosphatase or cholinesterase activities.

Case Number: DH-6

Type Subject: human

Authors: Koshelev et al. (1973) as cited by Gamaleya, pp. 118, 119

Exposure Target: Gp 1 = indolent wounds and trophic ulcers

Gp 2 = fractures of long bones

Experimental Controls:

Number of Subjects: 20/group

Laser Source: HeNe (2-40 mW) and UV-N (337.1 nm, 2 mW)

Beam Parameters:

Exposure/Treatment: Emission power density was "chosen individually"

Duration Exposure:

Treatment Schedule: Gp 1 = 15-33 sessions

Gp 2 = 20-24 sessions

Comments: "Stimulated healing" of Gp 1

"Accelerated callus formation" in Gp 2.

Case Number: DH-7

Type Subject: human

Authors: Mester et al. (1973) Acta Chir Acad Sci Hung 14:347-356 (also, as cited by Gamaleya, p. 119)

Exposure Target: GP 1 - crural ulcer caused by mechanical injury

GP 2 = X-ray therapy ulcers

Gp 3 = postthrombotic crural ulcer, medial and lateral aspects

Gp 4 = X-ray therapy ulcer on necrotic base

Experimental Controls: Gp 3 - medial side unirradiated at first, but subsequently irradiated

Number of Subjects: Gp 1 and 2 = 2 each, Gp 3 and 4 = 1 each

Laser Source: HeNe (Gp 1-3) and ruby (Gp 4)

Beam Parameters:

Exposure/Treatment: 1 J/cm² each (for Gp 3 treated 3x1-cm² area each time)

Duration Exposure:

Treatment Schedule: 2 times weekly

Comments: Gp 1 healed in 2-10 weeks (2 patients)

Gp 2 healed in 8 and 12 weeks (2 patients)

Gp 3 healed in 5 weeks; as lateral side healed saw signs of healing on medial (control) side as well, so irradiated it for 6 more weeks to complete healing

Gp 4 healed in 12 weeks. Assays indicated an increased collagen synthesis.

Case Number: DH-8

Type Subject: human

Authors: Odinets (1972) as cited by Gamaleya, pp. 121, 122

Exposure Target: Rheumatoid polyarthritis of 2-20-yr duration; 24/30 patients had proliferative joint changes; 6/30 patients were subacute

Experimental Controls:

Number of Subjects: 30

Laser Source: HeNe (20 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 20 s/joint, but \leq 4 min/total session

Treatment Schedule: 25-30 d

Comments: General condition improved

"Nearly half" patients increased movement and muscle strength

No significant changes seen in blood morphology or serum protein fractions.

Case Number: DH-9 Type Subject: human
Authors: Bogdanovich et al. (1973, 1974) as cited by Gamaleya, p. 122
Exposure Target: Gp 1 = arthritis deformans
Gp 2 = calcanean spurs
Gp 3 = osteochondrosis
Gp 4 = epicondylitis, periarthritis, etc.

Experimental Controls:

Number of Subjects: Gp 1 = 75; Gp 2 = 68; Gp 3 = 12; Gp 4 = 30

Laser Source: HeNe (10 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 10 min/site, but \leq 30 min/session

Treatment Schedule: 12-15 sessions

Comments: Pain and edema decreased

For some patients a "lasting beneficial effect could be obtained only after 2 or 3 courses of treatment, given at monthly intervals."

Case Number: DH-10 Type Subject: human
Authors: Mazo (1971) as cited by Gamaleya, p. 122
Exposure Target: Primary and secondary radiculitis; exposure site unspecified

Experimental Controls:

Number of Subjects: 101

Laser Source:

Beam Parameters:

Exposure/Treatment:

Duration Exposure:

Treatment Schedule:

Comments: "Favorable results."

Case Number: DH-11 Type Subject: human
Authors: Chenskikh et al. (1973) as cited by Gamaleya, p. 122
Exposure Target: Paralysis following spinal TB--irradiated point where peripheral motor nerves of lower limbs leave spinal cord

Experimental Controls:

Number of Subjects: 21

Laser Source:

Beam Parameters:

Exposure/Treatment:

Duration Exposure:

Treatment Schedule:

Comments: 19/21 had mobility "improved"

2/21 unchanged.

Case Number: DH-12

Type Subject: human

Authors: Korytnyi and Zazulevskaya (1970) as cited by Gamaleya, pp.122, 123

Exposure Target: Inflammatory-dystrophic periodontosis. Irradiated gums after removal of tartar and irrigation

Experimental Controls:

Number of Subjects: 44

Laser Source: HeNe (25 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: \leq 1 min/site, but \leq 10 min/session

Treatment Schedule: Daily sessions

Comments: "Most patients" reacquired pink gingival border and purulent discharge stopped

In 15/44 looseness of teeth decreased

In 18/44 no immediate changes were seen clinically, but all had improvement by a 1-month follow-up exam (oral hygiene procedures during this period are not given).

Case Number: DH-13

Type Subject: human

Authors: Askarova (1972) as cited by Gamaleya, p. 123

Exposure Target: Inflammatory-dystrophic periodontosis, stages I and II. Irradiated vestibular surface of gums

Experimental Controls:

Number of Subjects: 60

Laser Source: HeNe (20 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 5 s/site

Treatment Schedule: Daily for 10 d

Comments: Teeth became firmer, especially in less severe cases

Statistically significant increased biting pressure seen in all patients and in all groups of teeth except lower frontals.

Case Number: DH-14

Type Subject: human

Authors: Bakhtigaliev (1971) and Zazulevskaya et al. (1971) as cited by Gamaleya, p. 123

Exposure Target: Contents of pathological dentogingival pockets

Experimental Controls:

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment:

Duration Exposure:

Treatment Schedule:

Comments: Decreased number of microorganisms

Decreased pathogenicity of microorganisms

Increased phagocytosis.

Case Number: DH-15

Type Subject: human

Authors: Korytnyi (1971) and Baigurina (1972) as cited by Gamaleya, p. 123

Exposure Target: Chronic recurrent aphthous stomatitis; exposure site unspecified

Experimental Controls:

Number of Subjects: More than 60

Laser Source: HeNe (20-25 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure:

Treatment Schedule:

Comments: Pain relief noted after initial sessions

Healed a "few days sooner than ordinarily"

During next year no recurrence in 11 patients; other recurrences were less frequent than before treatment.

Case Number: MH-1

Type Subject: human

Authors: Chekurov et al. (1970) and Zav'yalova (1972) as cited by Gamaleya, p. 122

Exposure Target: Gp 1 = rheumatoid polyarthritis

Gp 2 = metabolic-dystrophic polyarthritis

Irradiated both affected joints and reflexogenic areas

Experimental Controls:

Number of Subjects: Gp 1 = 39; Gp 2 = 31

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment: $0.1-12 \text{ mW/cm}^2$

Duration Exposure: 1-30 s (increased with time and progress)

Treatment Schedule: Avg = 20 sessions

Comments: Initial exacerbation with 3-4 treatments--this subsided after 2-3 d

At end of sessions: 35/39 improved rheumatoid cases
4/39 no change rheumatoid cases

21 were called back for 2nd course--19 had improved in interim

Some improvement reported in all metabolic-dystrophic cases.

Case Number: MH-2

Type Subject: human

Authors: Chekurov et al. (1970) as cited by Gamaleya, p. 122

Exposure Target: Endarteritis obliterans. Irradiated site and reflexogenic zones

Experimental Controls:

Number of Subjects: 23

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment: $10-12 \text{ mW/cm}^2$

Duration Exposure: "One to several minutes"

Treatment Schedule: 20-d course

Comments: Initial exacerbation after 4-7 sessions, but this disappeared
General improvement seen at end, especially in a group with the spastic form of lesion of the limb arteries.

Case Number: IH-1

Type Subject: human

Authors: Bykhovskii and Khrebsov (1971) and Bykhovskii (1972) as cited by Gamaleya, pp. 123, 124

Exposure Target: Inflammatory condition of uterine adnexa. Irradiated reflexogenic and acupuncture points

Experimental Controls:

Number of Subject: 68

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment: 25 mW/cm²

Duration Exposure: 10-15 min to cover all points in that session

Treatment Schedule: 20-25 daily sessions

Comments: Some exacerbation with treatment

Of 30 women suffering flare-up inflammation:

17/30 cured

8/30 partial cure

5/30 no effect

The last 13/30 were given 10-15 extra sessions after 2-3 months and 10/13 were reportedly cured

Of 38 women with chronic inflammation: 27/38 cured

7/38 partial cure

4/38 no effect

Follow-up on 53 women showed a lasting cure.

Case Number: IH-2

Type Subject: human

Authors: Shchur et al. (1972) as cited by Gamaleya, p. 124

Exposure Target: Initial stage of arterial hypertension. Irradiated reflexogenic and acupuncture points

Experimental Controls:

Number of Subjects: 18

Laser Source: HeNe (20 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 10-30 s initially, increased to several minutes

Treatment Schedule: 12-25 sessions repeated, if necessary, after 25-50 d

Comments: In 10/18 blood pressure returned to normal

In 8/18 no immediate effect, though at a 10-30-d follow-up 4 were better.

Case Number: IH-3

Type Subject: human

Authors: Ermukhambetov (1971) as cited by Gamaleya, pp. 124, 125

Exposure Target: Stage II hypertension. Irradiated acupuncture points.
9/31 also received drugs.

Experimental Controls:

Number of Subjects: 31

Laser Source: HeNe (12 mW, with fiber light guide)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 10-20 s/session

Treatment Schedule: Daily for 10 d

Comments: "Hypotensive effect" observed in both groups, but more marked without drugs.

Case Number: IH-4

Type Subject: human

Authors: Utemuratova and Sokolova (1970) as cited by Gamaleya, p. 125

Exposure Target: Hypertension; exposure site unspecified

Experimental Controls:

Number of Subjects: 118

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment:

Duration Exposure:

Treatment Schedule:

Comments: 108/118 normalized blood pressure

10/118 unchanged

No significant abnormality of blood picture was seen.

Case Number: IH-5

Type Subject: human

Authors: Chatskii et al. (1972) as cited by Gamaleya, p. 125

Exposure Target: Hypertension of stages Ia, Ib, and IIa and 1-15-yr duration. Irradiated reflexogenic points (e.g. occipital region, solar plexus, knees, and soles of feet)

Experimental Controls:

Number of Subjects: 55

Laser Source: HeNe (16 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 5 s

Treatment Schedule: Single exposure (this is uncommon)

Comments: No significant change in arterial pressure.

Case Number: IH-6

Type Subject: human

Authors: Voronina (1972) and Voronina and Inyushin (1972) as cited by Gamaleya, p. 125

Exposure Target: Bronchial asthma of 2-24-yr duration and varying severity (3 groups). Irradiated different acupuncture points (segmental, meridian, and chronic)

Experimental Controls:

Number of Subjects: 21

Laser Source: HeNe (25 mW)

Beam Parameters:

Exposure/Treatment:

Duration Exposure: 40-60 s

Treatment Schedule: 10-20 daily sessions/course and 1-3 courses separated by 1-2 months

Comments: Using a spirographic test, all patients gave initial improvement and favorable short-term (6 mo) results

A parallel study showed decreased arterial oxygenation-- authors assume this is due to "activation of tissue respiration."

Case Number: IH-7

Type Subject: human

Authors: Shakirova and Inyuskin (1971) as cited by Gamaleya, p. 126

Exposure Target: Infantile cerebral palsy; exposure site unspecified

Experimental Controls:

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment:

Duration Exposure:

Treatment Schedule:

Comments: No results given.

Case Number: IH-8

Type Subject: human

Authors: Chekurov and Paremskaya (1972) as cited by Gamaleya, p. 126

Exposure Target: Inflammatory spinal cord disease; exposure site unspecified

Experimental Controls:

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment:

Duration Exposure:

Treatment Schedule:

Comments: No results given.

Case Number: IH-9

Type Subject: human

Authors: Kunin and Stolyar (1973) as cited by Gamaleya, p. 126

Exposure Target: "Certain mental diseases"; exposure site unspecified

Experimental Controls:

Number of Subjects:

Laser Source: HeNe

Beam Parameters:

Exposure/Treatment:

Duration Exposure:

Treatment Schedule:

Comments: No results given.

